

Variant: *NM_213599.3(ANO5):c.2503_2505del (p.Phe835del)*

Version: 1.0

CA242118 [↗](#)

195634 (ClinVar) [↗](#)

Gene: ANO5 ([HGNC:203859](#))

Condition: autosomal recessive limb-girdle muscular dystrophy
([MONDO:0015152](#))

Inheritance Mode: Autosomal recessive inheritance

UUID: 66985fba-19e3-49da-a0e9-4d02471dcc58

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HGVS expressions

NM_213599.3:c.2503_2505del

NM_213599.3(ANO5):c.2503_2505del (p.Phe835del)

NC_000011.10:g.22276182_22276184del

CM000673.2:g.22276182_22276184del

NC_000011.9:g.22297728_22297730del

CM000673.1:g.22297728_22297730del

NC_000011.8:g.22254304_22254306del

NG_015844.1:g.88007_88009del

ENST00000532043.2:n.520_522del

ENST00000682266.1:c.2053_2055del

ENST00000682341.1:c.2461_2463del

ENST00000683197.1:c.2372+1435_2372+1437del

ENST00000683411.1:c.2053_2055del

ENST00000683437.1:c.2053_2055del

ENST00000683613.1:n.3497_3499del

ENST00000684663.1:c.2458_2460del

ENST00000324559.9:c.2503_2505del

ENST00000648804.1:n.2838_2840del

ENST00000324559.8:c.2503_2505del

ENST00000532043.1:n.520_522del

NM_001142649.1:c.2500_2502del

NM_213599.2:c.2503_2505del

NM_001142649.2:c.2500_2502del

Likely Pathogenic

Met criteria codes 4

PM3_Strong

PP4

PM4

PM2_Supporting

Not Met criteria codes 22

BP5

BP7

BP4

BP3

BP1

BP2

PS1

PS2

PS3

PS4

PP1

PP2

PP3

PM6

PM1

PM5

PVS1

BA1

BS2

BS1

BS4

BS3

Evidence Links 0

Expert Panel

[Limb Girdle Muscular Dystrophy VCEP](#) [↗](#)

Criteria Specification Information

[↗](#) **Criteria Specification:** ClinGen Limb Girdle Muscular Dystrophy Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for ANO5 Version 1.0.0

[↗](#) **Criteria Specification Approval History**

[↗](#) **Criteria Specifications for this VCEP**

Limb Girdle Muscular Dystrophy VCEP

The NM_213599.3: c.2503_2505del variant in ANO5 is predicted to cause a change in the length of the protein due to an in-frame deletion of one amino acid in a non-repeat region, p.(Phe835del) (PM4). This variant has been detected with a pathogenic ANO5 variant in at least four individuals with LGMD, including confirmed in trans in one patient (c.191dup, 1 pt, ClinVar SCV000767093.6 internal data communication) and in unknown phase in two patients (c.2018A>G p.(Tyr673Cys), 0.5 pts, ClinVar SCV000767093.6 internal data communication; c.191dup, 0.5 pts, ClinVar SCV000574876.19 internal data communication) (PM3_Strong). At least one patient with this variant displayed progressive limb girdle muscle weakness (PP4). The filtering allele frequency of this variant is 0.000017531 (the upper threshold of the 95% CI of 12/1109046 exome chromosomes) in the European (non-Finnish) population in gnomAD v4.1.0, which is less than the ClinGen LGMD threshold ≤ 0.0001 for PM2_Supporting, meeting this criterion (PM2_Supporting). In summary, this variant meets the criteria to be classified as Likely Pathogenic for autosomal recessive limb girdle muscular dystrophy based on the ACMG/AMP criteria applied, as specified by the ClinGen LGMD VCEP (LGMD VCEP specifications version 1.0.0; 01/07/2025): PM4, PM3_Strong, PP4, PM2_Supporting.

Met criteria codes

PM3_Strong			This variant has been detected with a pathogenic ANO5 variant in at least four individuals with LGMD, including confirmed in trans in one patient (c.191dup, 1 pt, SCV000767093.6) and in unknown phase in two patients (c.2018A>G p.(Tyr673Cys), 0.5 pts, ClinVar SCV000767093.6 internal data communication; c.191dup, 0.5 pts, ClinVar SCV000574876.19 internal data communication) (PM3_Strong).
PP4			At least one patient with this variant displayed progressive weakness, which is specific for LGMD 2L (PP4_Supporting, internal laboratory data).
PM4			The c.2503_2505del variant is predicted to cause a change in the length of the protein (p.Phe835del) due to an in-frame deletion of 1 amino acid in a non-repeat region (PM4).
PM2_Supporting			The filtering allele frequency of this variant is 0.000017531 (the upper threshold of the 95% CI of 12/1109046 exome chromosomes) in the European (non-Finnish) population in gnomAD v4.1.0, which is less than the ClinGen LGMD threshold ≤ 0.0001 for PM2_Supporting, meeting this criterion (PM2_Supporting).

Not Met criteria codes

BP5			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP7			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP4			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

BP3		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP1		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP2		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PS1		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PS2		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PS3		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PS4		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PP1		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PP2		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PP3		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM6		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM1		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM5		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PVS1		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BA1		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

BS2		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS1		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS4		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS3		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

Curation History 

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